UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,443	11/16/2001	Hyam I. Levitsky	213026	1421

23460 7590 09/10/2002

LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6780

EXAMINER
CHEN, LIPING

ART UNIT	PAPER NUMBER
1632	4

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/992,443	Applicant(s) LEVITSKY ET AL.	
	Examiner Liping Chen	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,17-28,40-47 and 50-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,17-28,40-47 and 50-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the claims

Applicants' amendments, filed on 11/16/2001 (Pager No. 3) has been entered.

Claims 15, 16, 29-39, 48 and 49 are cancelled from further consideration pursuant to 37 C.F.R. 1.142(b).

Claims 1-14, 17-28, 40-47 and 50-53 are pending and examined in this office action on the merits.

Priority

This application is filed on 11/16/2001,
Which is a Con of 09/241,939, filed on 02/02/1999,
which claims benefit of 60/073,405, filed 02/02/1998.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14, 17-28, 40-47 and 50-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art

that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. In the instant case, while a written description for GM-CSF expressing K562 cell line (page 18-19, Example 1) is generally understood, there is no written description regarding to any cell or cell line that naturally lacks MHC-I and MHC-II, no written description regarding to any cell line that is characterized by the absence of B-lymphocyte markers of immunoglobulin, an Epstein-Barr virus genome and associated nuclear antigen and also lacks MHC-I and MHC-II (pertaining to instant claims 2 and18), no written description regarding to any human cell line that is derived from a blast crisis of chronic myeloid leukemia and lacks of MHC-I and MHC-II (pertaining to instant claim 3), there is also no written description regarding to the source of cells that lack MHC-I and MHC-II and can be used for the production of bystander cell lines. Although the specification provides direction of producing cells that lack MHC-I and MHC-II antigens and a reference (U.S. Patent

5,574,205) for inactivation of MHC-I and MHC-II antigen (specification, page 7, line12-30), it is not adequate written description pertaining to instant claims. Because the cells are required to naturally lack these antigens. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Furthermore, the applicant claims an improved method for cancer immunotherapy, there is no written description regarding to what is the improvement and to which specific cancer therapy area, the instant invention can be applied. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The

specification provided only the bovine sequence. In the instant case, as the skilled artisan can not envision if GM-CSF-expressing K562 cells express MHC-I and MHC-II or not from the written description, there is no written description regarding to any cell that naturally lacks MHC-I and MHC-II, the full breadth of the claim dose not meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-14, 17-28, 40-47 and 50-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is directed to a universal bystander cell line, which is a human cell line, naturally lacks MHC-I and MHC-II antigens, and comprises a nucleic acid sequence encoding GM-CSF, wherein the universal bystander cell line expressed about 500 ng or greater GM-CSF/10^6 cells/24 hours; Claims 2-14, 17-21, 40-47 and 50-53 are depending on claim 1 and further comprise different limitations such as different cell characters (claims 2-4), different GM-CSF expression level or culturing conditions (claims 5-14), a composition comprising the cell line (claims 17-21) a method of stimulating an immune response to a cancer in a human patient using the cell line (claims 40-48) and a improvement method of cancer immunotherapy (claims 50-53); claims 22-28 are directed to a method of making a universal bystander cell line.

The specification neither provides teaching or guidance as which cell or cell line naturally lacks MHC-I and MHC-II nor the source of obtaining the cell line. Although the specification provide a direction for producing cells that lack MHC-I and MHC-II antigens and a reference for inactivation of MHC-I and MHC-II antigen (specification, page 7, line12-30), there is no teaching or guidance as how to produce the cell instantly claimed. Moreover, the modified cells that lack MHC-I and MHC-II are not naturally lacking MHC-I and MHC-II. Although the specification provides an example of making GM-CSF-expressing K562 cells and compares the expression of MHC-I and MHC-II between GM-CSF-expressing K562 cells and Pro22 cells in Figure 2. However, there is no baseline provided so that it is hard to determine if GM-CSF-expressing K562 cells express MHC-I and MHC-II or not from the Figure, and there is also no related teaching or guidance provided. Further, the specification provide a list of cancers that can be treated using the instant invention such as carcinomas of the bladder, breast, colon, kidney, liver, lung ovary, pancreas, rectum and stomach (specification, page 17, line 15-21), there is no teaching as how to target different cancers, how to escape from immune response of the patient accepting the treatment to the bystander cell line so that introduced bystander cell line can continuously produce an immunomodulatory cytokine GM-CSF. Janeway et al. (Janeway-Travers, ImmunoBiology, Garland Publishing Inc, 1994) teaches that T lymphocytes act on cells of the body that contain foreign proteins by means of receptors that recognize antigen, not in its

intact form, as it is recognized by B cell, but rather as peptide fragments derived from the foreign proteins and bound to MHC (Janeway-Travers, page 1:24, first parag.). Although the bystander cell of instant invention is intended to lack MHC-I and MHC-II antigens, the cell itself is still a foreign antigen to any patient if the cell is not isolated from the patient receiving the therapy. The specification does not provide any teaching or guidance as how to reduce the host immune response to the bystander cells introduced. Verma et al. (Nature, 389:239-242, 1997) points out that the problems in current gene therapy are the lack of efficient delivery systems, lack of sustained expression and host immune reactions (Verma, page 239, col. 1). Further, the claim is also reads on xenograft transplantation. Parker et al. (Immunology Today, 17:373-378, 1996) teach the immunopathogenesis of xenograft rejection which includes termed acute vascular xenograft rejection or delayed xenograft rejection as the most immediate impediment to clinical application of xenotransplantation (page 373, bridg. Parag.). Although, the specification provides an example of making GM-CSF-expressing K562 cell line, there is no evidence that this cell line plays any role in stimulating an immune response to a cancer cell in a human patient or play any role in any specific cancer immunotherapy. The only *in vivo* example provided in the specification is using bystander cells derived form a C3H(H-2k) lymphoma (page 20, Example 2), that is irrelevant with the current invention. It is noted that case law requires that the disclosure of an application shall inform those skilled in the art how to use applicants' alleged discovery, not

how to find out, how to use it, for themselves (see In re Gardner et al. 166 USPQ 138 (CCPA 1970). The specification only teaches what is intended to be done, but does not actually teach how to do that which is intended.

As the specification fails to provide guidance as which cell lacks MHC-I and MHC-II, lack of evidence and guidance of using any bystander cell line that lacks MHC-I and MHC-II or using GM-CSF-expressing K562 cell line in a method of cancer immunotherapy, lack of guidance for targeting each specific cancer cells, the claimed methods are not enabled. Due to the nature of the invention, the state of the prior art, the lack of direction and guidance, no evidence the GM-CSF-expressing K562 cell line described can improve cancer immunotherapy, no teaching or guidance as how to prevent immune response to hetologous bystander cell line for gene therapy, the claimed invention would have required one skilled in the art to engage in an undue amount of experimentation without a predictable degree of success to achieve any specific and the breath of the invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liping Chen, whose telephone number is (703) 305-4842. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time). Should the examiner be unavailable,

inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Pauline Farrier, Patent Analyst, at (703) 305-3550. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-8724.

Liping Chen, Ph.D.
Patent Examiner
Group 1632

DEBORAH J. REYNOLDS
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600